

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 December 2002 (27.12.2002)

PCT

(10) International Publication Number
WO 02/102852 A3

(51) International Patent Classification⁷: **C07K 14/705**,
C12N 15/12, 15/79, 5/10, A61K 38/17, 31/7088, A61P
37/00

(21) International Application Number: PCT/GB02/02743

(22) International Filing Date: 14 June 2002 (14.06.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0114533.3 14 June 2001 (14.06.2001) GB

(71) Applicant (for all designated States except US): **AVIDEX LIMITED** [GB/GB]; 57C Milton Park, Milton Park OX14 4RX (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **JAKOBSEN, Bent, Karsten** [DK/GB]; Avidex Limited, 57C Milton Park, Milton Park OX14 4RX (GB). **GLICK, Meir** [IL/US]; 11 Catano Avenue #307, Morristown, NJ 07960 (GB).

(74) Agents: **LEE, Nicholas, John** et al.; Kilburn & Strode, 20 Red Lion Street, London WC1R 4PJ (GB).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
18 December 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODIFIED CD8 MOLECULE, NUCLEIC ACID ENCODING SAID MOLECULE, AND THEIR THERAPEUTIC USE

(57) Abstract: The present invention provides modified CD8 molecules whose binding to MHC is enhanced compared to wild type CD8, wherein Ser₅₃ of at least one CD8 α chain thereof is mutated to another amino acid. It also provides nucleic acids encoding such molecules, and to the use of such molecules and nucleic acids in immunosuppressive therapy, in particular as inhibitors of cytotoxic T cell responses.



WO 02/102852 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/02743

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 C12N15/12 C12N15/79 C12N5/10 A61K38/17
 A61K31/7088 A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 21576 A (GERTH ULRICH CONRAD ; JAKOBSEN BENT KARSTEN (GB); GAO GEORGE FU (GB) 6 May 1999 (1999-05-06) the whole document ---	1-21
A	GAO G F ET AL: "Molecular interactions of coreceptor CD8 and MHC class I: the molecular basis for functional coordination with the T-cell receptor" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 12, 1 December 2000 (2000-12-01), pages 630-636, XP004225441 ISSN: 0167-5699 cited in the application the whole document --- -/--	1-21

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

7 October 2003

Date of mailing of the international search report

23/10/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Lechner, O

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/02743

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SEWELL A K ET AL: "Antagonism of cytotoxic T-lymphocyte activation by soluble CD8." NATURE MEDICINE. UNITED STATES APR 1999, vol. 5, no. 4, April 1999 (1999-04), pages 399-404, XP002255511 ISSN: 1078-8956 the whole document ---	1-21
A	KERN P S ET AL: "Structural basis of CD8 coreceptor function revealed by crystallographic analysis of a murine CD8alphaalpha ectodomain fragment in complex with H-2Kb." IMMUNITY. UNITED STATES OCT 1998, vol. 9, no. 4, October 1998 (1998-10), pages 519-530, XP002255512 ISSN: 1074-7613 the whole document ---	1-21
A	LI S ET AL: "Identification of the CD8 DE loop as a surface functional epitope. Implications for major histocompatibility complex class I binding and CD8 inhibitor design." THE JOURNAL OF BIOLOGICAL CHEMISTRY. UNITED STATES 26 JUN 1998, vol. 273, no. 26, 26 June 1998 (1998-06-26), pages 16442-16445, XP002255513 ISSN: 0021-9258 the whole document -----	1-21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 02/02743

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 19 (only as far as relating to an in vivo method) and 20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 02/02743

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9921576	A	06-05-1999	AT 215833 T	15-04-2002
			AU 752910 B2	03-10-2002
			AU 9637498 A	17-05-1999
			CA 2308463 A1	06-05-1999
			CN 1283120 T	07-02-2001
			DE 69804839 D1	16-05-2002
			DE 69804839 T2	10-10-2002
			DK 1024822 T3	05-08-2002
			EP 1024822 A1	09-08-2000
			ES 2175798 T3	16-11-2002
			WO 9921576 A1	06-05-1999
			HK 1031099 A1	13-12-2002
			JP 2001521005 T	06-11-2001
			NO 20002148 A	27-06-2000
			NZ 504240 A	26-11-2002
			PT 1024822 T	30-09-2002